

FEB 27 2007

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TO:	FACSIMILE:	TELEPHONE:
U.S. Patent and Trademark Office Attn: Examiner T. Wessendorf Art Unit: 1639	(571) 273-8300	(571) 272-0812

FROM: Kate H. Murashige - Reg No. 29,959

DATE: February 27, 2007

Number of pages with cover page: 14

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**Comments:**

ATTORNEY DOCKET: 388512010101  
GROUP ART UNIT: 1639  
EXAMINER: T. Wessendorf  
SERIAL NO.: 10/678,414  
FILING DATE: October 2, 2003  
INVENTOR(S): Lawrence M. KAUVAR, et al.  
TITLE: MULTIHUE LABELS

**Papers attached:**

Please find a copy of the response that was filed on October 13, 2006, along with a copy of the stamped receipt postcard showing it was received on October 16, 2006. Examiner Wessendorf does not have a copy of this response and we are merely supplying the attached copy for your file. Thank you.

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SD-360961

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FEB 27 2007

Inventor: Lawrence M. KAUVAR et al.

Atty Docket No.: 388512010101

Application No.: 10/678,414  
Title: MULTIHUE LABELS

Filing Date: October 2, 2003

Documents Filed:

Transmittal (1 page)  
Fee Transmittal (1 page + duplicate)  
Amendment Under 37 C.F.R. § 1.111 (7 pages)  
Terminal Disclaimers (2 pages)

COPY

Via: First Class Mail  
Sender's Initials: KHM1/xxv2

Date: October 13, 2006

Inventor: Lawrence M. KAUVAR et al.

Atty Docket No.: 388512010101

Application No.: 10/678,414  
Title: MULTIHUE LABELS

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Transmittal (1 page)  
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Terminal Disclaimers (2 pages)



Via: First Class Mail  
Sender's Initials: KHM1/xxv2

Date: October 13, 2006

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PTO/SB/21 (09-04)

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<h1 style="text-align: center;">TRANSMITTAL FORM</h1> <p style="text-align: center;">(to be used for all correspondence after initial filing)</p>		Application Number	10/878,414
		Filing Date	October 2, 2003
		First Named Inventor	Lawrence M. KAUVAR
		Art Unit	1639
		Examiner Name	T. Wessendorf
Total Number of Pages In This Submission	12	Attorney Docket Number	388512010101

## ENCLOSURES (Check all that apply)

<input checked="" type="checkbox"/> Fee Transmittal Form (1 page + duplicate for fee processing) <input type="checkbox"/> Fee Attached <input checked="" type="checkbox"/> Amendment Under 37 CFR § 1.111 (7 pages) <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input checked="" type="checkbox"/> Terminal Disclaimers (2 pages) <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD	<input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): Return Receipt Postcard
Remarks: _____ Customer No. 25225 <div style="font-size: 2em; opacity: 0.5; transform: rotate(-10deg); display: inline-block;">COPY</div>		

## SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	MORRISON & FOERSTER LLP		
Signature	<i>Kate H. Murashige</i>		
Printed name	Kate H. Murashige		
Date	October 13, 2006	Reg. No.	29,959

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to: MS Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: October 13, 2006

Signature: *Roberta Vinson* (Roberta Vinson)

sd-340202

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PTO/SB/17 (01-06)

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<b>FEE TRANSMITTAL</b> For FY 2006		<b>Complete if Known</b>	
		Application Number	10/678,414
<input checked="" type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27		Filing Date	October 2, 2003
		First Named Inventor	Lawrence M. KAUFAR
		Examiner Name	T. Wessendorf
		Art Unit	1639
TOTAL AMOUNT OF PAYMENT		(\$)	130.00
		Attorney Docket No.	388512010101

**METHOD OF PAYMENT (check all that apply)**

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<input checked="" type="checkbox"/> Charge fee(s) indicated below		<input type="checkbox"/> Charge fee(s) indicated below, except for the filing fee		
<input checked="" type="checkbox"/> Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17		<input checked="" type="checkbox"/> Credit any overpayments		

**FEE CALCULATION (All the fees below are due upon filing or may be subject to a surcharge.)****1. BASIC FILING, SEARCH, AND EXAMINATION FEES**

Application Type	FILING FEES		SEARCH FEES		EXAMINATION FEES		Fees Paid (\$)
	Fee (\$)	Small Entity Fee (\$)	Fee (\$)	Small Entity Fee (\$)	Fee (\$)	Small Entity Fee (\$)	
Utility	300	150	500	250	200	100	0.00
Design	200	100	100	50	130	65	0.00
Plant	200	100	300	150	160	80	0.00
Reissue	300	150	500	250	600	300	0.00
Provisional	200	100	0	0	0	0	0.00

**2. EXCESS CLAIM FEES****Fee Description**

Each claim over 20 (including Reissues)

Each independent claim over 3 (including Reissues)

Multiple dependent claims

Total Claims	Extra Claims	Fee (\$)	Fee Paid (\$)	Multiple Dependent Claims	Fee (\$)	Fee Paid (\$)
HP	HP	HP	0.00	HP	HP	0.00
Indep. Claims	Indep. Claims	Indep. Claims	0.00	Indep. Claims	Indep. Claims	0.00

**3. APPLICATION SIZE FEE**

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee (\$)	Fee Paid (\$)
HP	HP	HP	HP	0.00

**4. OTHER FEE(S)**

Non-English Specification, \$130 fee (no small entity discount)

Other (e.g., late filing surcharge): 2814 Statutory Disclaimer (2 @ 65 ea.)

130.00

<b>SUBMITTED BY</b>		Registration No.	29,959	Telephone	(858) 720-5112
Signature	<i>Kate H. Murashige</i>	(Attorney/Agent)		Date	October 3, 2006
Name (Print/Type)	Kate H. Murashige				

sd-340198

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PTO/SB/17 (01-06)

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Fees pursuant to the Consolidated Appropriations Act, 2005 (P.L.R. 4818).

**FEE TRANSMITTAL**  
For FY 2006**Complete if Known**

Application Number	10/678,414
Filing Date	October 2, 2003
First Named Inventor	Lawrence M. KAUVAR
Examiner Name	T. Wessendorf
Art Unit	1639
Attorney Docket No.	388512010101

☒ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT (\$) 130.00

**METHOD OF PAYMENT** (check all that apply)☐ Check ☐ Credit Card ☐ Money Order ☐ None ☐ Other (please identify):☒ Deposit Account Deposit Account Number: 03-1952 Deposit Account Name: Morrison & Foerster LLP

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☒ Charge fee(s) indicated below☐ Charge fee(s) indicated below, except for the filing fee☒ Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17☒ Credit any overpayments**FEE CALCULATION** (All the fees below are due upon filing or may be subject to a surcharge.)**1. BASIC FILING, SEARCH, AND EXAMINATION FEES**

Application Type	FILING FEES		SEARCH FEES		EXAMINATION FEES		Fees Paid (\$)
	Fee (\$)	Small Entity Fee (\$)	Fee (\$)	Small Entity Fee (\$)	Fee (\$)	Small Entity Fee (\$)	
Utility	300	150	500	250	200	100	0.00
Design	200	100	100	50	130	65	0.00
Plant	200	100	300	150	160	80	0.00
Reissue	300	150	500	250	600	300	0.00
Provisional	200	100	0	0	0	0	0.00

**2. EXCESS CLAIM FEES****Fee Description**

Each claim over 20 (including Reissues)

Each independent claim over 3 (including Reissues)

Multiple dependent claims

Small Entity	
Fee (\$)	Fee (\$)
50	25
200	100
360	180

Total Claims	Extra Claims	Fee (\$)	Fee Paid (\$)
HP	x	=	0.00

HP = highest number of total claims paid for, if greater than 20.

Indep. Claims	Extra Claims	Fee (\$)	Fee Paid (\$)
HP	x	=	0.00

HP = highest number of independent claims paid for, if greater than 3.

**3. APPLICATION SIZE FEE**

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee (\$)	Fee Paid (\$)
- 100 =	/50	(round up to a whole number) x	=	0.00

**4. OTHER FEE(S)**

Non-English Specification, \$130 fee (no small entity discount)

Other (e.g., late filing surcharge): 2814 Statutory Disclaimer (2 @ 65 ea.)

130.00

**SUBMITTED BY**

Signature	Kate H. Murashige	Registration No. (Attorney/Agent)	29,959	Telephone	(858) 720-5112
Name (Print/Type)	Kate H. Murashige	Date	October 3, 2006		

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**For Fee Processing**

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Dated: October 13, 2006

Signature: Roberta Vinson

Roberta Vinson

said Docket No.: 388512010101  
(PATENT)

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Lawrence M. KAUVAR, et al.

Application No.: 10/678,414

Filed: October 2, 2003

For: MULTIHUE LABELS

Confirmation No.: 9986

Art Unit: 1639

Examiner: Teresa D. Wessendorf

AMENDMENT UNDER 37 C.F.R. § 1.111

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

COPY

Dear Sir:

This is in response to an Office Action herein, mailed 25 August 2006, time for response to which was set to expire 25 November 2006. Claims 43-47 and 50-51 were examined and rejected. Claims 48-49 were withdrawn from consideration, but would be rejoined if a generic claim were allowed. Careful consideration has been given to the grounds for rejection, and the following amendment and discussion are offered in response. Reconsideration is respectfully requested.

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Application No.: 10/678,414

Docket No.: 388512010101

CLAIM AMENDMENTS

1-42. (canceled)

43. (currently amended): A particulate label which comprises

(a) a particulate support having a diameter of no more than 100 nm to which particle is bound to at least three fluorophores, wherein each said fluorophore emits a detectable signal different-distinguishable from that emitted by the others and wherein the magnitude-ratio of intensities of each of said emitted signals provides a distinctive hue-and-wherein the magnitude of the signal emitted by each said fluorophore may be varied; and

(b) wherein said particulate support is coupled to a reagent coupled to said particulate support.

44. (previously presented): The label of claim 43, wherein the particulate support is a latex bead.

45. (previously presented): The label of claim 43, wherein the reagent is an antibody or fragment thereof, a peptide generated from a cDNA library, a substance in a combinatorial chemistry library, or an oligonucleotide.

46. (previously presented): The label of claim 43, wherein the reagent is coupled to the particulate support by a covalent linkage.

47. (previously presented): The label of claim 46, wherein the covalent linkage is a disulfide or carboxamide linkage.

48. (withdrawn): The label of claim 43, wherein the reagent is linked to the particulate support by a non-covalent linkage.

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Application No.: 10/678,414

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49. (withdrawn): The label of claim 48, wherein the non-covalent linkage is an epitope/antibody linkage, or a histidine/chelated NI linkage, or comprises an agar layer in which reagent is trapped.

50. (currently amended): A spatially defined arrangement of a multiplicity of particulate different labels of claim 43, wherein each label is characterized by a ~~different hue~~ distinguishable from the hue of different labels, and each different particulate support is bound to a different reagent.

51. (previously presented): The arrangement of claim 50, which is displayed on a surface to permit determination of the spatial position of said labels.

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Application No.: 10/678,414

Docket No.: 388512010101

REMARKS

Claim 43 has been amended in response to the rejection under 35 U.S.C. § 112, paragraph two. Support for this amendment is found, for example, on page 10 of the specification, which discusses the signals in terms of their intensities. The requirement that the signals be distinguishable is clear in that the various colors emitted can be distinguished from each other, as described in the paragraph on page 10, beginning at line 11 and Figure 2 referred to therein. Support for the ratio of intensities is also found in this paragraph. See, e.g., line 17 on page 10. The remainder of the amendment is editorial. Claim 50 has been similarly clarified. Accordingly, no new matter has been added. Entry of the amendment is respectfully requested.

Applicants have found that it is possible to couple three or more fluorophores to a very small particle having a diameter of no more than 100 nm. To applicants' knowledge, this is the first disclosure of such small and efficient particulate labels.

Double-Patenting

Applicants believe the double-patenting rejection is improperly based on consideration of the specifications of the cited documents rather than the claims *per se* as is the appropriate referent for such assessment. However, in order to expedite prosecution, terminal disclaimers with respect to U.S. 6,492,125 and U.S. 6,642,062 are enclosed.

The Rejections Under 35 U.S.C. § 112, Paragraph Two

All claims were rejected under this statutory section. Claim 43 has been extensively amended in response. By separating the particulate support bearing the fluorophores from the reagent that is coupled thereto into separate paragraphs, it is believed that the claim is clarified. The

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Application No.: 10/678,414

Docket No.: 388512010101

particulate label contains both the particulate support and the reagent. The term "magnitude" has been replaced by "intensity" which is believed clear, and the term "different" is replaced by the functionally meaningful "distinguishable." It is believed, therefore, that the objections of the Office have been met.

Claim 50 is asserted to be a duplicate of claim 43. This basis for rejection is not understood. Claim 43 requires only a single particulate label; claim 50 requires an arrangement of a multiplicity of different particulate labels and they must be spatially arranged so that they can be separately identified.

Similarly, claim 51 further limits claim 50 because the spatial arrangement must be on a surface – not within a three-dimensional volume.

Accordingly, this basis for rejection may properly be withdrawn.

#### The Rejection Under 35 U.S.C. § 102

All claims were rejected as assertedly anticipated by Chee, *et al.*, U.S. patent 7,033,754. Applicants believe the rejection is in error for the following reason.

The present application is a continuation of U.S. Serial No. 09/146,984 filed 3 September 1998 – *i.e.*, U.S. patent 6,642,062 cited by the Office. Therefore, the only § 102(e) date that can be asserted for Chee, *et al.*, is that of provisional application number 60/090,473 filed 24 June 1998. All of the remaining documents from which Chee, *et al.*, claim priority are later than the filing date of the parent herein. It is unclear from the present record whether the provisional application that might properly be cited anticipates the present invention. However, according to the copy of the application available on PAIR, it appears that microspheres as small as 100 nm are not disclosed. Page 10, beginning at line 30, describes bead sizes from 500 nm to millimeter size

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Application No.: 10/678,414

Docket No.: 388512010101

and a preferred lower dimension of 200 nm. What appears to be the corresponding portion in the issued patent, at column 10, specifies 100 nm/ml, unlike the provisional which specifies 500 nm/ml.

Applicants would appreciate an analysis of provisional 60/090,473 which might properly be cited against the present application as opposed to the issued parent which, unless supported by the provisional, is not. Since the provisional application can be read and printed only one page at a time on PAIR, a copy of this application would be helpful in evaluating its disclosure.

In that regard, it would be helpful to have portions of the text more precisely identified than what appears to be approximately 20 pages of specification (column 9-column 32).

In view of the apparent failure of the provisional application to anticipate, this basis for rejection may properly be withdrawn.

#### The Rejection Under 35 U.S.C. § 103

Respectfully, as this rejection requires the combination of Chee, which is not properly cited, with additional documents, this rejection may be withdrawn for the reasons set forth above.

#### Conclusion

Terminal disclaimers have been submitted to overcome the double-patenting rejection. The claims have been amended to overcome the rejection under 35 U.S.C. § 112, paragraph two. It does not appear that the earliest priority document of the primary reference, Chee, discloses the particulate labels of the invention. Thus, it is believed all grounds for rejection are overcome and passage of pending claims 43-47 and 50-51 to issue, along with claims 48-49 which may be rejoined, is respectfully requested.

Application No.: 10/678,414

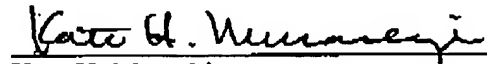
Docket No.: 388512010101

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket No. 388512010101.

Respectfully submitted,

Dated: October 13, 2006

By:



Kate H. Murashige  
Registration No. 29,959  
MORRISON & FOERSTER LLP  
12531 High Bluff Drive  
Suite 100  
San Diego, California 92130-2040  
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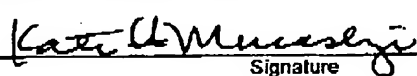
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PTO/SB/26 (09-04)

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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<b>TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT</b>	<b>Docket Number (Optional)</b> <b>388512010101</b>
<p>In re Application of: <u>Lawrence M. KAUVAR et al.</u></p> <p>Application No.: <u>10/678,414</u></p> <p>Filed: <u>October 2, 2003</u></p> <p>For: <u>MULTIHUE LABELS</u></p> <p>The owner, <u>Trellis Bioscience, Inc.</u>, of <u>100</u> percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of prior patent No. <u>6,492,125</u> as the term of said prior patent is defined in 35 U.S.C. 154 and 173, and as the term of said prior patent is presently shortened by any terminal disclaimer. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patent are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.</p> <p>In making the above disclaimer, the owner does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term as defined in 35 U.S.C. 154 and 173 of the prior patent, "as the term of said prior patent is presently shortened by any terminal disclaimer," in the event that said prior patent later:</p> <ul style="list-style-type: none"> <li>expires for failure to pay a maintenance fee;</li> <li>is held unenforceable;</li> <li>is found invalid by a court of competent jurisdiction;</li> <li>is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;</li> <li>has all claims canceled by a reexamination certificate;</li> <li>is reissued; or</li> <li>is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.</li> </ul> <p>Check either box 1 or 2 below, if appropriate.</p> <p>1. <input type="checkbox"/> For submissions on behalf of a business/organization (e.g., corporation, partnership, university, government agency, etc.), the undersigned is empowered to act on behalf of the business/organization.</p> <p>I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.</p> <p>2. <input checked="" type="checkbox"/> The undersigned is an attorney or agent of record. Reg. No. <u>29,959</u></p> <div style="display: flex; justify-content: space-between; margin-top: 10px;"> <div style="text-align: center;">         Signature     </div> <div style="text-align: center;"> <u>October 13, 2006</u>        Date     </div> </div> <div style="text-align: center; margin-top: 10px;"> <u>Kate H. Murashige</u>        Typed or printed name     </div> <div style="text-align: right; margin-top: 10px;"> <u>(858) 720-5112</u>        Telephone Number     </div> <p><input checked="" type="checkbox"/> Terminal disclaimer fee under 37 CFR 1.20(d) is included.</p> <p><small>*Statement under 37 CFR 3.73(b) is required if terminal disclaimer is signed by the assignee (owner). Form PTO/SB/86 may be used for making this certification. See MPEP § 324.</small></p>	

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PTO/SB/26 (09-04)

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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**TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING  
REJECTION OVER A "PRIOR" PATENT**

Docket Number (Optional)

388512010101

In re Application of: Lawrence M. KAUVAR et al.

Application No.: 10/878,414

Filed: October 2, 2003

For: MULTIHUE LABELS

The owner, Trellis Bioscience, Inc., of 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of prior patent No. 6,842,062 as the term of said prior patent is defined in 35 U.S.C. 154 and 173, and as the term of said prior patent is presently shortened by any terminal disclaimer. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patent are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the owner does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term as defined in 35 U.S.C. 154 and 173 of the prior patent, "as the term of said prior patent is presently shortened by any terminal disclaimer," in the event that said prior patent later

expires for failure to pay a maintenance fee;

is held unenforceable;

is found invalid by a court of competent jurisdiction;

is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;

has all claims canceled by a reexamination certificate;

is reissued; or

is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

Check either box 1 or 2 below, if appropriate.

1. ☐ For submissions on behalf of a business/organization (e.g., corporation, partnership, university, government agency, etc.), the undersigned is empowered to act on behalf of the business/organization.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

2. ☒ The undersigned is an attorney or agent of record. Reg. No. 29,959

Kate H. Murashige  
Signature

October 13, 2006  
Date

Kate H. Murashige  
Typed or printed name

(858) 720-5112  
Telephone Number

- ☒ Terminal disclaimer fee under 37 CFR 1.20(d) is included.

\*Statement under 37 CFR 3.73(b) is required if terminal disclaimer is signed by the assignee (owner).  
Form PTO/SB/96 may be used for making this certification. See MPEP § 324.